High-throughput screening in primary neurons.

Journal: Methods Enzymol

Publication Year: 2012

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PubMed link: 22341232

Funding Grants: Gladstone CIRM Scholars Program, Gladstone CIRM Scholar Program

Public Summary:

Scientific Abstract:
Despite years of incremental progress in our understanding of diseases such as Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS), there are still no disease-modifying therapeutics. The discrepancy between the number of lead compounds and approved drugs may partially be a result of the methods used to generate the leads and highlights the need for new technology to obtain more detailed and physiologically relevant information on cellular processes in normal and diseased states. Our high-throughput screening (HTS) system in a primary neuron model can help address this unmet need. HTS allows scientists to assay thousands of conditions in a short period of time which can reveal completely new aspects of biology and identify potential therapeutics in the span of a few months when conventional methods could take years or fail all together. HTS in primary neurons combines the advantages of HTS with the biological relevance of intact, fully differentiated neurons which can capture the critical cellular events or homeostatic states that make neurons uniquely susceptible to disease-associated proteins. We detail methodologies of our primary neuron HTS assay workflow from sample preparation to data reporting. We also discuss the adaptation of our HTS system into high-content screening (HCS), a type of HTS that uses multichannel fluorescence images to capture biological events in situ, and is uniquely suited to study dynamical processes in living cells.